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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/887,784	06/19/2001	Sara Petersen Bjorn	0459-0615P	8714
2292	7590	11/05/2003	EXAMINER	
BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			ROBINSON, HOPE A	
			ART UNIT	PAPER NUMBER

1653

DATE MAILED: 11/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application N .</b> 09/887,784	<b>Applicant(s)</b> BJORN ET AL.	
	<b>Examiner</b> Hope A. Robinson	<b>Art Unit</b> 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 01 August 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1-6,8,9,11,12,20 and 21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                    | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

1. Applicant's response to the Office Action mailed June 17, 2003 on August 1, 2003 is acknowledged.

#### ***Claim Disposition***

2. Claims 20-21 have been added. Claim 7 has been canceled. Claims 1, 2 and 12 have been amended. Claims 1-6 and 8-21 are pending. Claims 1-9, 11-12 and 20-21 (SEQ ID NO: 4) are under examination.
3. It is noted that applicant provided arguments to support the traversal of the restriction requirement which have been fully considered. Regarding the election of SEQ ID NO: 4 and the withdrawal of claim 10, applicant's response states that the common feature between SEQ ID NOS: 4 and 8 are the point mutations, however, a single amino acid change can result in a different protein product, thus, the two sequences are separate and distinct. Should applicant state on the record that a reference that anticipates or renders obvious one sequence would also anticipate or render obvious the other sequence then both sequences will be searched. With regards to the restriction of originally presented claims 1-19, applicant states that no burden of search exists. Under *In re Ochiai*, if applicant has an allowable product claim then methods of using the product will be rejoined, however, the claims directed to the second product the nucleic acid will not be rejoined as the protein and DNA are patentably distinct as set forth in the previous Office Action. The two products are structurally distinct and have separate modes of operation. The issues raised in the response have been fully addressed, however, not persuasive, thus the restriction requirement is deemed proper and final.

4. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

5. The following grounds of rejection are or remain applicable:

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:  
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-9, 11-12 and 20-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because the claim recites "wherein the amino acid in position 1 preceding the chromophore has been mutated" and there is no indicia of how position 1 is mutated. Note that the claim describes a mutation at position 222 only. The dependent claims hereto are also included in this rejection.

Claim 2 remains indefinite as a specific sequence must be provided that corresponds to the recited range, and please note that dependent upon the elected sequence the actual residue positions may differ. The recitation of a reference sequence corresponding to the recited residue position is necessary in the claim to clarify the "derived from" language recited in independent claim 1.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103 (a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102 (f) or (g) prior art under 35 U.S.C. 103 (a).

8. Claims 1-6 and 8 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Thastrup et al. (WO 97/11094 March 27, 1997) in view of Ehrig et al. (FEBS Letters, vol. 367, pages 163-166, 1995).

Thastrup et al. teach a fluorescent protein derived from GFP (Aequorea green fluorescent protein) or any functional analogue thereof wherein the amino acid in position 1 preceding the chromophore has been mutated to provide an increase of fluorescence intensity. Thastrup et al. teach that the proteins exhibit high fluorescence in cells expressing them when said cells are incubated at a temperature of 30 degrees or above. Thastrup et al. also teach that the chromophore is in position 65-67 and the substitution of F at position 64 for an aliphatic amino acid (see pages 1-4, claims 1-4 of the instant application). Thastrup et al. teach that the preferred

mutation is F64L (claims 5-6), however, deletions, substitutions, insertions or posttranslational modifications immediately preceding the chromophore are also included in the invention, however is silent on the E222G mutation recited in claim 1 of the instant specification.

However, Ehrig et al. teach the E222G mutation (see abstract, claims 1 and 8). Ehrig et al. teach a single amino acid change producing a mutant of GFP (E22G).

Therefore, it would have obvious for one of ordinary skill in the art at the time the invention was made to modify the teachings of Thastrup et al. (GFP mutation F64L) by adding in the teachings of Ehrig et al. (GFP E222G) to arrive at the claimed invention as a whole. One of ordinary skill in the art would be motivated to combine the teachings of the references because Thastrup et al., disclose that other mutations are possible preceding the chromophore provided that they result in improved fluorescence properties of the various fluorescent proteins (page 4, lines 10-15) and Ehrig teach such a mutation. Thus, the claimed invention was obvious to make and use at the time it was made and was *prima facie* obvious.

The response filed on August 1, 2003 states that reconsideration is requested for the rejections made under 35 U.S.C. 112, second paragraph. Note that the correction of the typographical error in claim 2 resulted in the withdrawal of that rejection, however, claim 2 remains rejected because applicant did not address the second part of the rejection. The residue positions recited in claim 2 are not tied to a reference sequence which needs to recited in the claims, thus the claim is unclear with respect to what is the protein that is only derived in independent claim 1. With regard to the rejection under 35 U.S.C. 103(a), applicant's comments have been considered. Note that the rejection has been clarified. The reference of record by

Tsien et al. has been withdrawn as Tsien et al. only reported the findings of Ehrig et al. thus this reference has been cited which is of record in the application. As stated above Ehrig rectifies the silent teaching of Thastrup et al. with regard to the point mutation found at E222 and teaches the substitution of E to G, thus rendering obvious the claimed invention.

### *Conclusion*

9. No claims are presently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope Robinson whose telephone number is (703) 308-6231. The examiner can normally be reached on Monday-Friday from 9:00 am to 6:30 pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S. F. Low, can be reached at (703) 308-2923.


Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-4242. Please affix the examiner's name on a cover sheet attached to your communication should you choose to fax your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).




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Art Unit: 1653

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Hope Robinson, MS 

Patent Examiner

  
**CHRISTOPHER S. F. LOW**  
**SUPERVISORY PATENT EXAMINER**  
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